containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of five immediate containers.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency*. Use either of the following methods:

(i) *Microbiological turbidimetric assay*. Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Dilute an accurately measured representative aliquot of the sample with sufficient distilled water to obtain a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *Spectrophotometric assay*. Reconstitute the sample as directed in the labeling and dilute a 1.0-milliliter aliquot in sufficient distilled water to obtain a solution containing 20 micrograms of chloramphenicol per milliliter. Dissolve an accurately weighed portion of the working standard in sufficient distilled water to obtain a solution containing 20 micrograms per milliliter. Using a suitable spectrophotometer and distilled water as the blank, determine the absorbance of the sample and standard solutions at 278 nanometers. Calculate the potency of the sample as follows:

$$\text{Milligrams of chloramphenicol per milliliter} = \frac{\text{Absorbance of sample} \times \text{labeled potency per milliliter in milligrams}}{\text{Absorbance of standard}}$$

(2) *Sterility*. Proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(1) of that section.

(3) *pH*. Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 5 milligrams per milliliter.

[49 FR 6093, Feb. 17, 1984, as amended at 50 FR 19921, May 13, 1985]

§ 455.310c Chloramphenicol ointment (chloramphenicol cream).

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Chloramphenicol ointment is chloramphenicol in a suitable and harmless ointment base, with or without suitable and harmless buffer substances, dispersing and suspending agents. It may contain cortisone or a suitable derivative of cortisone. If such base is water-miscible, it shall contain a suitable and harmless preservative. Its potency is not less than 1.0 milligram per gram. If it is intended for ophthalmic use, it is sterile. The chloramphenicol used conforms to the requirements of § 455.10a(a)(1), except paragraphs (a)(1) (ii), (iii), and (v) of that section. The chloramphenicol used in making the chloramphenicol ophthalmic ointment conforms to the requirements of § 455.10a(a)(1), except paragraphs (a)(1) (iii) and (v) of that section. Each other substance used, if its name is recognized in the U.S.P. or N.F., conforms to the standards prescribed therefor by such official compendium.

(2) *Packaging*. Unless it is packaged in a single dose container, chloramphenicol ointment shall be packaged in collapsible tubes, which shall be well-closed containers as defined by the U.S.P., and shall not be larger than the ⅛-ounce size if such ointment is represented for ophthalmic use, and in no case larger than the 2-ounce size, except that if it is labeled solely for hospital use it may be packaged in immediate containers of glass which meet the test for tight containers as defined by the U.S.P. The composition of the immediate container and closure shall be such as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in

applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(3) *Labeling.* In addition to the labeling requirements prescribed by § 201.100 of this chapter (regulations issued under section 502(f) of the act), each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the outside wrapper or container and the immediate container the statement ''Expiration date _____'', the blank being filled in with the date that is 60 months, or 24 months if it is packaged in an immediate container other than tin or glass, or 12 months if the ointment base is water miscible, after the month during which the batch was certified.

(ii) If it contains one of the active ingredients specified in paragraph (a)(1) of this section, after the name ''chloramphenicol ointment'', wherever it appears, the name of the active ingredient, in juxtaposition with such name.

(4) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(*a*) The chloramphenicol used in making the batch for potency, pH, specific rotation, melting point, and absorptivity.

(*b*) The batch for potency and for sterility if the ointment is intended for ophthalmic use.

(ii) Samples required:

(*a*) The chloramphenicol used in making the batch: 10 packages, each containing approximately 300 milligrams.

(*b*) The batch:

(*1*) For all tests except sterility: A minimum of 5 immediate containers if it is packaged in immediate containers of tin or glass; a minimum of 20 immediate containers if it is packaged in immediate containers other than tin or glass.

(*2*) For sterility testing: 20 immediate containers, collected at regular intervals throughout each filling operation.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows:

(i) *If the ointment is water miscible.* Place an accurately weighed representative portion of the sample into a high-speed glass blender jar containing 1.0 milliliter polysorbate 80 and sufficient distilled water to obtain a stock solution of convenient concentration. Blend for 3 to 5 minutes. Further dilute an aliquot of the stock solution with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated).

(ii) *If the ointment is not water miscible.* Place an accurately weighed representative portion of the sample into a separatory funnel containing approximately 50 milliliters of petroleum ether. Shake the sample and ether until homogeneous. Add 20 to 25 milliliters of distilled water and shake well. Allow the layers to separate. Remove the aqueous layer and repeat the extraction procedure with each of three more 20- to 25-milliliter quantities of distilled water. Combine the aqueous extractives in a suitable volumetric flask and dilute to volume with distilled water. Remove an aliquot and further dilute with distilled water to the reference concentration of 2.5 micrograms of chloramphenicol per milliliter (estimated). The potency of chloramphenicol ointment is satisfactory if it contains not less than 90 percent and not more than 130 percent of the number of milligrams of chloramphenicol that it is represented to contain.

(2) *Sterility.* If the ointment is intended for ophthalmic use, proceed as directed in § 436.20 of this chapter, using the method described in paragraph (e)(3) of that section. However, if the ointment is not soluble in isopropyl myristate proceed as directed in § 436.20 of this chapter, using the method described in § 436.20(e)(2), except use 100 milligrams in lieu of 300 milligrams of solids.

[39 FR 19166, May 30, 1974, as amended at 41 FR 10886, Mar. 15, 1976; 44 FR 10380, Feb. 20, 1979; 48 FR 3961, Jan. 28, 1983; 50 FR 19921, May 13, 1985]